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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,707	01/11/2001	Ira H. Pastan	15280-3561US	3958

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,707	PASTAN ET AL.	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,19-24 and 52-103* is/are pending in the application.

4a) Of the above claim(s) *19-24,59-67 and 79-103* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,52-58 and 68-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed on 10-12-2004 are acknowledged. Claims 1, 52, and 57 have been amended. Claims 1-11, 19-24 and 52-103 are pending. Claims 19-24, 59-67 and 79-103 remain withdrawn from consideration as being drawn to non-elected inventions. Claims 1-11, 52-58 and 68-78 are currently under examination.

Objections Withdrawn

The objection to the specification for failing to contain an abstract of the disclosure as required by 37 CFR 1.72(b) is withdrawn.

Objections Maintained

The objection to the specification for referring to U.S. patent Applications that have since been issued is maintained. Applicant's arguments refer to amendments not of record. Amendments addressing this issue were part of the amendment filed on 12-12-2003 (which was not entered) and were not incorporated in the amendment filed on 10-12-2004.

The objection to the specification for disclosing that SEQ ID NO:1 is the sequence of both the intact 3b3 antibody and a 3b3(Fv) is maintained for reasons of record. Applicant's arguments refer to amendments not of record. Amendments addressing this issue were part of the amendment filed on 12-12-2003 (which was not entered) and were not incorporated in the amendment filed on 10-12-2004.

Claim Rejections Withdrawn

The rejection of claims 1 and 52 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "a minimum binding affinity of 3B3" is withdrawn in light of the amendment thereto.

The rejection of claim 57 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "FV("dsFv") is withdrawn in light of the amendment thereto.

The rejection of claims 1-11, 52-56 and 38-74 and 77-78 under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bera et al. (Molecular Medicine Vol. 4, 1998, pages 384-391) is withdrawn. Applicant's arguments have been fully considered and deemed persuasive.

The rejection of claims 57-58 and 75-76 under 35 U.S.C. 103(a) as being unpatentable over Bera et al. (Molecular Medicine Vol. 4, 1998, pages 384-391) in view of Pastan et al. (U.S. Patent 6,147,203) is withdrawn. Applicant's arguments have been fully considered and deemed persuasive.

The rejection of claims 1-3, 6, 11, 57, 68-69, 72 and 75 under 35 U.S.C. 102(b) as being anticipated by Matsushita et al. (Aids Research and Human Retroviruses Vol. 6 No. 2, 1990, pages 193-203) is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 8, 10, 55-56, 58, 74, 76 and 78 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained for reasons of record.

Applicant argues:

1. The specification sets forth the sequences for the V_H and V_L sequences (SEQ ID NO: 1 and 2) of 3b3(fv).

2. PE38 is explicitly defined in the specification as a "truncated *Pseudomonas* exotoxin composed of amino acids 253-364 and 381-608.

3. Applicant's prior work and the art in general would provide the skilled artisan with the ability to form disulfide-stabilized Fvs, conjugating antibodies to effector molecules and the expression of antibody-cytotoxin constructs as fusion proteins.

Applicant's arguments have been fully considered and deemed non-persuasive.

The specification, contrary to Applicant's assertion does not explicitly define what sequences and linkers comprise either 3b3(Fv) or 3B3(dsFv). Both are deemed to be a unique singular entity comprising a V_H and a V_L sequence and a specific linker (if one was used). Applicant argues that the specification discloses the use of SEQ ID NO:1 and SEQ ID NO:2 in conjunction with an *exemplar* linker. The fact that the linker, as pointed out by Applicant, is variable, there is no **unique** sequence associated with the identifier 3b3(Fv).

With regard to Point 3, while the skilled artisan would be able to form disulfide-stabilized Fvs, there is no specific disclosure as to which amino acids in the 3B3 antibody need to be replaced with cysteines when forming the 3B3(dsFv). Consequently, the specific sequence associated either both 3b3(Fv) or 3B3(dsFv) is not known.

As stated previously, since it is apparent that antibodies 3b3(Fv) and 3B3(dsFv) as well as immunotoxins 3B3(Fv)-PE38 and 3B3(dsFv)-PE38 are required in order to practice the invention. The deposit of biological material is considered by the Examiner to be necessary for the enablement of the current invention (see 37 CRF 1.808(a)). The rejected claims all recite said biological material in a manner suggesting they each constitute a single entity. Since the specification provides no sequences for said material and one of skill in the art would not be able to discern what V_H and V_L sequences of the 3B3 antibody are incorporated into the claimed 3B3(Fv) or 3B3(dsFv), deposit of the aforementioned biological material is required.

If the deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit, or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the following criteria have been met:

1) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent; and

3) the deposits will be maintained for a term of at least thirty (30) years from the date of the deposit or for the enforceable life of the patent or for a period of at least five (5) years after the most recent request for the furnishing of a sample of the deposited material, whichever is longest; and

4) a viability statement in accordance with the provisions of 37 CFR 1.807; and

5) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 CRF 1.809(d) should be added to the specification. See 37 CFR 1.803 – 1.809 for additional explanation of these requirements.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-6, 8-9, 11, 52-55,57, 68-72 and 74-77 under 35 U.S.C. 103(a) as obvious over Matsushita et al. (Aids Research and Human Retroviruses Vol. 6 No. 2, 1990, pages 193-203) in view of Barbas et al. (PNAS Vol. 91, 1994, pages 3809-3813 – IDS-5) and Pastan et al. (U.S. Patent 5,458,878 – IDS-5) is maintained for reasons of record.

Applicant argues:

1. Developments in the art after the date of Matsushita's publication would destroy the *prima facie* case of obviousness outlined in the rejection.

Applicant's arguments have been fully considered and deemed non-persuasive.

Applicant's arguments are predicated on references that are not germane to the instant invention. The instant invention is drawn to immunotoxins comprising a cytotoxin (e.g. PE38) attached to an anti-gp120 antibody (e.g. 3B3) having the binding specificity of 3B3. Said antibody is a dsFv. The instant invention is also drawn to kits and compositions comprising said immunotoxins.

The Ramachandran et al. reference is drawn to CD4-PE40 immunotoxins which are not analogous to the instant invention. Hence any "results" based on the Application of said immunotoxin would not have any bearing on the perceived efficacy of immunotoxin based on the combination of the cited references.

The Davey et al. reference is drawn to sCD4-PE40 immunotoxins which are not analogous to the instant invention. Hence any "results" based on the Application of said immunotoxin would not have any bearing on the perceived efficacy of immunotoxin based on the combination of the cited references.

The Goldstein et al. reference was published in 2000, which was after the invention "was made" and hence would not have been part of the art at the time the invention was made.

As outlined previously, Matsushita et al. disclose anti-pg120 immunotoxins comprising the 0.5ϑ antibody coupled to the *Pseudomonas* exotoxin (see abstract). Matsushita et al. differs from the instant invention in that they don't disclose the use of the 3B3 antibody or the use of altered PE40. Barbas et al. disclose a human antibody to gp120 (3B3) with broad strain cross-

reactivity (see page 3812-3813). Pastan et al. disclose modifications of the carboxyl terminus of the PE molecule resulting in increased cytotoxicity (see abstract and column 3, line 27 to column 4, line 10). Given that Matsushita et al. suggest the use of an antibody that is broadly reactive with a number of HIV isolates (see page 200), it would have been obvious for one of ordinary skill in the art to use the 3B3 antibody in the immunotoxin disclosed by Matsushita et al. Moreover, it would a have been equally obvious for one of ordinary skill to incorporate the PE modifications disclosed by Pastan et al. in order to take advantage of the resulting increase in cytotoxicity. It should be noted that while the incorporation of immunotoxins in kits is not explicitly disclosed by Matsushita et al., said incorporation would have been obvious to one of ordinary skill in the art in order to reduce cost and ease preparation time.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
April 11, 2005

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